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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,725	02/28/2005	Hitoshi Okamoto	P26510	8296

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EXAMINER	
MAKAR, KIMBERLY A	
ART UNIT	PAPER NUMBER
1636	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	04/23/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 04/23/2007.

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Office Action Summary	Application No.	Applicant(s)	
	10/525,725	OKAMOTO ET AL.	
	Examiner	Art Unit	
	Kimberly A. Makar, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *9-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Claims 1-13 are pending. Claims 9-13 are withdrawn. A response to aplicant's remarks can be found below. Any rejection not mentioned in this office action is withdrawn, rendering applicant's arguments moot.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in

the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

4. The instant claims, construed as discussed herein above, embrace an isolated regulatory element that is capable of enhancing gene expression efficiency in a motor or sensory neuron, wherein the structural characteristics of the claimed regulatory element are essentially unlimited.

5. The Guidelines for Written Description state: "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (Federal Register, Vol. 66, No. 4, Column 3, page 1106). "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus" (MPEP §2163(3)(a)(ii)).

6. The Guidelines further state, "[s]atisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the genus in view of the species disclosed" (Id. at 1106, column 3).

7. In the instant case, the application discloses 6 sequences, which, based on the discussion in Examples 1-4 is presumed to be genomic DNA upstream of the 5'

upstream genomic neuronal-specific enhancer sequence for the zebrafish, human, mouse, and pufferfish Islet-1 gene. However, there is no demonstration in the disclosure that the sequences set forth as SEQ ID NO: 1-6 as defined by the broad claims 1, 2, 4 and 5 is sufficient to drive transcription in any or all motor or sensory neuronal cells as recited in the claim. Claims 1, 2, 4 and 5 are broad and read on any sequence capable of eliciting the same enhancing capabilities of the SEQ IDs listed in the claims by deletion, substitution or addition of one to thirty nucleotides. Is the limitation directed at limiting the changes to 30 nucleotides, such that only individual nucleotides are changed? Or can multiple regions be deleted, as long as the individual region is no longer than 30 nucleotides? The claimed nucleotide sequences are hundreds of base pairs long. There is no teaching of which thirty base pairs are to be changed, or how to determine which nucleotides should be altered. The deletion or addition or substitution of even a single nucleotide has the potential to disrupt the enhancer function of the claimed SEQ ID NO. Therefore, it is not clear that the claimed alterations of the sequences set forth in the sequence listing in the claims are actually species of the invention.

8. Even if one is to assume, *arguendo*, that the functional properties recited in the instant claims are inherent to the nucleic acids set forth as SEQ ID NO: 1-6, these species are not representative of the broad genus claimed because they clearly do not convey the necessary common attributes or features of essentially any nucleic acid having the recited function.

9. Furthermore, with regard to the "relevant identifying characteristics" of the claimed invention, the specification provides no disclosure of the structural features that define the function recited in the claims. As stated in MPEP 2163(I)(A), a biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes. Thus, applications that seek to claim biological molecules having a defined function and broadly divergent structure must disclose a correlation between that function and a corresponding structure. Although example 2 identifies high homology between SEQ ID NO: 1-4 in base pairs 235-560, 204-528, 206-530 and 211-555 respectively there is no evidence that these specific sequences are sufficient to define a genus wherein these sequences comprises a "deletion, substitution or addition of one to thirty nucleotides" is capable of driving transcription in any or all motor or sensory neuronal cells as presently claimed. Therefore, the application also fails to provide the relevant identifying characteristics of the claimed invention.

10. An adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. It is not sufficient to define DNA solely by its principal biological property (i.e., it is capable of driving transcription in a neuronal-specific manner) because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what

that material consists of, is not a description of that material. Thus, claiming all DNA's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

11. In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention because it does not provide adequate written description for the broad class of a nucleotide sequence of SEQ ID NO: 1-6 in which deletion, substitution or addition of one to thirty nucleotides is capable of driving transcription in a motor or sensory neuron beyond the scope of a nucleic acid selected from the group consisting of a nucleic acid consisting of SEQ ID NO: 1-6. Therefore, the claims are properly rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description. This rejection is maintained from the office action dated 10/31/06.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1, 2,4,and 5 recite the phrase "stringent conditions." This phrase is not defined in the claims nor in the specification. How "stringent" is stringent? The ability of a nucleic acid molecule to hybridize will vary depending upon a variety of factors in including nucleic acid length, nucleotide content (G/C content) as well as temperature, detergents, etc. What factors are involved in determining "stringent conditions?" Is

there are degree of homology that determines stringent conditions? If so, what? The specification teaches a teaching on "hybridizing under stringent conditions to a nucleotide sequence complementary to the nucleotide sequence as shown in any one of SEQ ID NOs: 1 to 6" on page 11 of the instant specification. However, the instant claims are directed toward fragments, and derivatizations of SEQ ID's NO 1-6. Would not the "stringent conditions" therefore have to change in order to maintain hybridization? There is no teaching on how to adjust the hybridization depending upon the alteration in sequences or fragments thereof. A skilled artisan would be unable to determine the metes and bounds of the claimed invention.

Response to Arguments

14. Applicant's arguments filed 1/31/07 have been fully considered but they are not persuasive. Applicant's amend claims 1-8 to recite the phrase "deletion,, substitution, or addition or one to thirty nucleotides and capable of enhancing gene expression efficient in motor neurons" and that these claims no longer read on any sequence with the claimed function. "as amended, the claims are limited to the a sequence claimed with up to 30 deletions, substitutions or additions" and that these is fewer than 5% of the bases in the sequence (see page 1 of applicant's remarks). Applicant also submits that the instant specification defines the claimed genus of nucleic acid sequence capable of driving transcription in any or all motor or sensory neurons, and particularly points to regions 235-560 or SEQ ID NO: 1, 204-528 of SEQ ID NO: 2, 206 – 530 of SEQ ID NO:

3, and 211-333 of sequence SEQ ID NO: 4 as regions which function as enhancers for improving gene expression efficiency in motor neurons, along with a region of high homology between SEQ ID NO 5 and 6 is suggested to be the enhancer region for these SEQ ID NOs. Further applicant's assert that the areas of homology function as enhancer for improving gene expression efficiency in motor neurons, thereby establishing a common feature with an associated common function among the sequences (page 2 of applicant's remarks).

15. As noted above, the limitation of "up to 30 deletions, substitutions or additions" is indefinite. There is no disclosure if these deletions, substitutions or additions are to a single nucleotide, or a region of the original sequence? A single deletion could encompass 98% of the original sequence, which reads on more than 5% of the bases in the original sequences. A single deletion of a single nucleotide could abalate enhancer function.

16. Any alteration of "up to 30 deletions, substitutions or additions" to the regions or SEQ ID 1-6 could alter the function of the enhancer nucleotides. Applicant has shown no examples of mutagenesis of these regions to suggest that such alterations result in enhancer properties. In specific regard to SEQ ID NOs 5-6, these sequences were predicted to have enhancer function solely by sequence homology; they have not been reduced to practice to show if SEQ ID NOs 5-6 without any mutations, deletions or substitutions has any actual enhancer function in motor neurons. Thus a claim directed to SEQ ID NOs 5-6 in which mutations deletions or substitutions to sequences would still have enhancer function would require a high degree of experimentation.

17. Therefore, a genus of enhancers represented by SEQ ID NO 1-6 in which "up to 30 deletions, substitutions or additions" made to either the entire region of SEQ ID 1-6 or a smaller fraction of the sequences including bases 235-560 or SEQ ID NO: 1, bases 204-528 of SEQ ID NO: 2, bases 206 – 530 of SEQ ID NO: 3, and bases 211-333 of sequence SEQ ID NO: 4 would not necessarily have the enhancer function claimed. Therefore, the 112 1st written description rejection over claims 1-8 is maintained for reasons of record in the office action 10/31/06 and the reasons above.

Conclusion

18. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Makar, Ph.D. whose telephone number is 571-272-4139. The examiner can normally be reached on 8AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kam/04/09/07

DAVID GUZO
PRIMARY EXAMINER